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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/616,659	07/09/2003	Costas D. Maranas	P06367US03	9959

27407 7590 08/28/2007  
MCKEE, VOORHEES & SEASE, P.L.C.  
ATTN: PENNSYLVANIA STATE UNIVERSITY  
801 GRAND AVENUE, SUITE 3200  
DES MOINES, IA 50309-2721

EXAMINER

SKOWRONEK, KARLHEINZ R

ART UNIT	PAPER NUMBER
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1631

MAIL DATE	DELIVERY MODE
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08/28/2007

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Advisory Action</b> <b>Before the Filing of an Appeal Brief</b>	Application No.	Applicant(s)	
	10/616,659	MARANAS ET AL.	
	Examiner	Art Unit	
	Karlheinz R. Skowronek	1631	

**--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

THE REPLY FILED 16 August 2007 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:

- a) ☐ The period for reply expires \_\_\_\_\_ months from the mailing date of the final rejection.  
b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### NOTICE OF APPEAL

2. ☒ The Notice of Appeal was filed on 08-16-2007. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

#### AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because  
(a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);  
(b) ☐ They raise the issue of new matter (see NOTE below);  
(c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or  
(d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: \_\_\_\_\_. (See 37 CFR 1.116 and 41.33(a)).

4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).  
5. ☐ Applicant's reply has overcome the following rejection(s): \_\_\_\_\_.  
6. ☐ Newly proposed or amended claim(s) \_\_\_\_\_ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).  
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☒ will not be entered, or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.  
The status of the claim(s) is (or will be) as follows:  
Claim(s) allowed: \_\_\_\_\_.  
Claim(s) objected to: \_\_\_\_\_.  
Claim(s) rejected: 1-5, 7, 8, 10-14, and 18-20.  
Claim(s) withdrawn from consideration: 6, 9 and 15-17.

#### AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).  
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing of good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).  
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

#### REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because:  
See Continuation Sheet.  
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08) Paper No(s). \_\_\_\_\_.  
13. ☐ Other: \_\_\_\_\_.

Continuation of 11. does NOT place the application in condition for allowance because: Regarding applicants' argument that the priority document 60/395,763 ('763) provides adequate written description and enabling disclosure is not persuasive. Although as applicant points out the '763 application recites, "a computational framework is developed", the disclosure fails to provide enabling written support for one of ordinary skill to make the invention. The '763 disclosure also fail to provide enabling written support to make the MILP-based formulation alluded to in the '763 specification at page 3, line 7-9.

Regarding applicants arguments with respect to the rejection of claim 1 under 35 USC 112, first paragraph for lack of scope of enablement have been considered and are not persuasive. Applicants argue that not all optimization problems are being claimed but rather only optimization problems that couple two objective functions. This is not persuasive because claim 1 recites an optimization problem having 1 or more cellular objectives in line 5. an optimization problem that couples 2, 5, 100, 1000 cellular objectives or any number of 1 or greater of cellular objectives is claimed. Therefore the optimization problem formed when 5 cellular objective are selected means that optimization problem with 6 objectives (5 cellular and 1 bioengineering) is formed and not an optimization with 2 objectives as argued by applicant. Applicant argues that the reliance on Papin et al is unfounded because the teachings of Papin are not pertinent to the mathematical optimization problems. This is not persuasive because the convex analysis is a branch of mathematics that is used to analyze systems of in equalities (p. 252,col. 2, par 1 line 4). Papin teaches the suitability of convex analysis in determining elementary modes the maximum theoretical yield of a particular product, reading on an optimization problem (p. 252, col. 2, para 1, line 17-23). Papin continues that development of the elementary modes using convex analysis are used to identify optimal and suboptimal yields of aromatic amino acids from carbohydrate substrates (p256, col. 1, para. 1, line 6-9). Therefore, the reliance on Papin is not unfounded.

Regarding applicants arguments with respect to the rejection of claims 1-5,7-8,10-14 and 18-20 under 35USC103 as being obvious over Burgard et al, in view of Yang et al and in further view of Voit et al. Applicant argues the combinations of references does not teach the limitation of coupling a cellular objective with a bioengineering objective and argue the references separately. This is not persuasive for the reasons of record. Voit et al teach the application of linear programming optimization methods and show a bilevel optimization problem to optimize the yield of the bioengineering objective while maintaining the cellular objective of steady state. Burgard et al show a computational method to flux balance analysis by solving an optimization problem to maximize the production the 20 amino acids and maintaining growth on glucose and acetate.

*John S. Brusca 24 August 2007*  
JOHN S. BRUSCA, PH.D.  
PRIMARY EXAMINER